were nearly the same, suggesting that high concentrations of ultrafine particles were present during both sets of exposures. There were methodological differences between the two sets of exposures; however the results suggest that the ultrafine components of PM2.5 may be more strongly associated with the observed decreases in resistance in the PM-exposed developing lung than are larger-sized particle components.

Executive Summary

Background

The Children's Health Study (CHS), which was conducted by the University of Southern California for the ARB, has reported that NO_2, acid vapor, fine ambient particles and elemental carbon exposures during the period of lung growth and development in Southern California children were associated with impaired lung function growth, increased school absences, and exacerbated asthma (Kunzli et al. 2003). An earlier study by Frischer and colleagues had shown that long term exposure to ambient ozone (O_3) was associated with reduced pulmonary function growth (Frischer et al. 1999), however O_3 was not associated with pulmonary function growth deficits in the CHS (Gauderman et al. 2004a). In reviewing the CHS data, Tager suggested that the decrease in some measures of lung function growth might also have been associated with summertime levels of SO_2, NO_2 and PM10 (Tager 1999).

Specific Aims

This study had 5 specific aims:

1. Examine effects of eight week exposure to a high concentration of concentrated PM2.5 on the development of lung function and capacity in mice exposed from the time that they are weaned through 11 weeks of age (adulthood).
2. Examine the role of oxidative stress in PM-induced lung injury and pulmonary function decrements in Nrf2-/- mice.

3. Determine whether the effect of exposure to concentrated PM2.5 from weaning to adulthood on pulmonary function decrements persists once exposure ends.
4. Obtain tissue, blood, and bronchoalveolar lavage samples to examine effects of PM2.5 exposure during the period of lug growth and development on expression of growth and development-related genes in the lungs.
5. Contrast differences in lung function and lung growth as a function of particle concentration and particle composition.

To accomplish these specific aims we used an animal model; mice were exposed to concentrated ambient fine particles (CAPs) during the animal's period of rapid growth and development (weeks four through twelve). The particle concentrator does not concentrate gases or vapors. The concentrator removes up to 70% of nitrogen oxides and most of ambient ozone. Because the concentrator particle inlet is size-selective, this study could specifically address the question of whether PM2.5 exposure was responsible for lung function growth deficits, with little interference from other covariable air pollutants.

Results

Exposure of mice to CAPs at high concentration (mean concentration 243 $\mu g/m^3$) supports the conclusions of the CHS study; namely that PM2.5 exposure could lead to decreased pulmonary function growth (increased resistance and decreased compliance) in animals exposed from weaning to adulthood. The study also showed that the changes persisted up to a week after exposure ended. Animals exposed to a lower CAPs concentration (mean concentration 56 $\mu g/m^3$) during the same age range showed a similar increase in pulmonary resistance but did not show the reduction in compliance that was observed in the high concentration study, suggesting that PM2.5 concentration is a factor in influencing lung function growth. Overall, the results of this study suggest that PM2.5 exposure can adversely influence lung function growth, since other pollutants were removed, or at least greatly reduced, by the operation of the particle concentrator.

Discussion

We were unable to completely address all of the objectives of the project. Studies with the genetically modified mice were only partially successful because the animals did not breed well, and proved to be too frail to withstand the exposure and pulmonary function measurement protocols. They were also more variable in their pulmonary function responses than had been anticipated. In addition, due to a Governor's Executive Order putting all state contracts on hiatus for three months, an experiment had to be terminated prior to its completion, and then repeated once the hiatus was lifted. Because of this, monies were not available to perform all planned analyses. Tissue samples for histology, and blood and bronchoalveolar lavage fluid for analysis of oxidative and inflammatory mediators, and for gene array analyses have been stored for subsequent analyses when funding becomes available. In addition, the hiatus contributed to the reduced effort for the planned experiment using the Nrf2-/- mice because funding was not available to support continued maintenance and breeding of these mice.

Conclusions

The major conclusion of this study is that PM exposure, independent of other pollutants, can impede the development of pulmonary function in a growing mammal and that deficit persists for at least two weeks after the termination of exposure. There were two sets of exposures; the first exposures were performed at 'high' concentration (PM2.5, 243 $\mu g/m^3$; number concentration, 93,000 particles/cc) and the second exposures were at 'low' concentration, (PM2.5 56 $\mu g/m^3$; particle number 83,000 particles/cc). Both studies produced significant increases in resistance. Particle mass concentrations in the low study were nearly $1/5^{th}$ that in the high study, however the particle number concentrations were nearly the same, suggesting that high concentrations of ultrafine particles were present during both sets of exposures. Although there were methodological differences between the two sets of exposures, the results suggest that the ultrafine components of PM2.5 may be more strongly associated with the